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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/753,079	01/08/2004	Bao-Lu Chen	PP18459.005	6553

27476 7590 11/22/2005

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Intellectual Property - R440  
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EXAMINER

KIM, YUNSOO

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 11/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/753,079	CHEN ET AL.	
	Examiner	Art Unit	
	Yunsoo Kim	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 2 September 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1 and 4-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 4-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>9/2/05</u> .  | 6) <input type="checkbox"/> Other: _____                                    |

### DETAILED ACTION

1. Applicants' response and amendment filed on 9/2/05 is acknowledged.  
Claims 1, 7, 12, 18 and 20 have been amended.  
Claims 2-3 have been canceled.
  2. Applicants' IDS filed on 9/2/05 has been acknowledged.
  3. In view of Applicants' amendments and cancellation of claims, the previous rejections set forth under 35 U.S.C. 112 first and second paragraphs (sections 5-7 of action mailed 5/3/05) have been withdrawn.
  4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:  

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.
- This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
5. Claims 1 and 4-21 stand rejected under 35 U.S.C. 103 as being unpatentable over Andya et al. (U.S.Pat. 6,267,958 B1, of record) in view of Chen et al. (U.S.Pat. No. 5,888,968, IDS ref, of record) for the reasons set forth in the office action mailed 5/3/05.

Applicants' arguments filed on 9/2/05 have been fully considered but they are not persuasive.

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Applicants traversed the rejection based on the teachings of the '958 patent are only suitable for highly soluble aqueous proteins and not suitable for the highly insoluble protein like TFPI, and no motivation to combine teachings of '968 and '958 patents to benefit from lyophilization.

Unlike Applicants' arguments, the '958 patent includes insoluble proteins like lipoproteins (col. 6, lines 44-47, col. 6-7 overlapping paragraph) would encompass by the stable lyophilized formulation.

Furthermore, the '968 patent teaches various combinations of buffer including Na Acetate, Na Citrate comprising glycine, sucrose, imidazole, and/or NaCl in table 1, with solubility more than 10mg/ml (Table 1, col. 7, lines 25, 29 and 39).

As it is taught by the '958 patent, freeze-drying (lyophilization) is a commonly employed technique to improve stability, storage, delivery and multi-use formulation (col. 1, lines 42-60).

It is examiner's position that the combinations of teaching remain obvious to improve storage conditions of the composition.

From the combined teachings of references, one of ordinary skill in art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary skill in the art at the time the invention was made, as evidenced by references, especially in the absence of evidence to the contrary.

6. The following new ground of rejection is necessitated by the Applicants' provision of IDS filed on 9/2/05.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1 and 4-21 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/24814 (IDS reference).

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The '814 publication teaches stable liquid formulation comprising TFPI, buffering agent at 10mM (i.e. citric acid, succinate, p. 59, lines 13-18), amino acid at 100-300mM (i.e. L-arginine, p. 59, lines 13-25) at pH 5.5, with TFPI concentration at 0.15mg/ml (p. 59, claims 1-36, p. 4-5, Fig Description 9-11, p. 13. lines 14-25). Given molecular weight of 174g of Arginine, 300mM is equivalent to 3%.

The '814 publication further teaches the above stable liquid formulation can also be lyophilized in order to increase the storage stability (claims 37-39, p. 8, lines 8-16).

Claim 17 is included in this rejection as the '814 publication teaches combining sugar and/or sugar alcohol (i.e. mannitol or sucrose) at concentration between 2-10% (p. 16-17 overlapping paragraph) with stable formulation.

As the referenced formulation and the claimed formulation of buffer comprising amino acid are identical, the characteristic of formulation having greater than 96% of stability is inherent property. Thus, reference teachings anticipate the claimed invention.

9. No claims are allowable.

10. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 9/2/05 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on Monday thru Friday 8:30 - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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November 3, 2005

  
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